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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/665,472	09/20/2000	Menzo Havenga	4489US	8505

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EXAMINER	
LEFFERS JR, GERALD G	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 12/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/665,472	HAVENGA ET AL.	
	Examiner	Art Unit	
	Gerald G Leffers Jr.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 September 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This is the first action on the merits for the instant application. Claims 1-22 are pending and under consideration in the instant application.

Information Disclosure Statement

Receipt is acknowledged of a submission filed 9/20/00 in which, consistent with the duty to disclose information material to patentability (37 CFR 1.56 and 1.175), applicants have disclosed the existence of a related application (i.e. 09/573,740). The examiner has reviewed the file for the co-pending, related application. However, the submission filed 9/20/00 is not an information disclosure statement (IDS), and has not been treated as such. It would be inappropriate to cite a co-pending, non-published application on any patent that issues from the instant claims.

Drawings

New corrected drawings are required in this application because of the objections made on the PTO Form 948 mailed along with the instant office action. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance (see 37 CFR 1.85(a).

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c). The address for Abraham Bout has been altered.

Specification

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

In the instant specification, the word “means” appears. Appropriate correction is required.

Claim Objections

Claim 2 is objected to because of the following informalities: it is grammatically incorrect in that the word “a” is missing between the words “by” and “viral”. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-18, 20-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Each of the claims is directed towards a gene delivery vehicle having at least a tissue tropism for dendritic cells where the dendritic cells is provided by a capsid protein. In the broadest claim, claim 1, the gene delivery vehicle can be of any type (e.g. a liposome, a positively-charged protein/DNA complex, a nucleic acid-coated projectile, a car, etc.). In the remaining claims, the invention comprises a gene delivery vehicle comprising a capsid that itself comprises fragments derived from at least two different viruses. In these more narrowly drawn claims, there is no limitation that the capsid be an adenoviral capsid, only that at least one of the viral protein fragments be derived from an adenoviral capsid. In the most narrowly drawn of the rejected claims, at least one of the protein fragments is derived from an adenoviral fiber protein. Even in these more narrowly drawn claims, there is no limitation that the capsid is necessarily an adenoviral capsid. Thus, in each of these claims the gene delivery vehicle can be any viral vector of any type (e.g. phage, plant viral vectors and any viral vector that infects animal cells). Therefore, each of the claims comprises an enormously broad genus of gene delivery vehicles that must somehow have been provided a tissue tropism for dendritic cells.

The instant specification is entirely directed towards adenoviral vectors wherein the fiber protein from a subgroup B adenovirus (e.g. Ad11, Ad16, Ad35 or Ad51) or Ad40L has been inserted in place of the native fiber protein. There is no description in the instant specification of any other capsid type comprising a dendrite-specific ligand such that the hybrid vector comprises a tissue tropism for dendritic cells. No basis is provided in the instant specification for one of skill in the art to envision what such non-adenoviral gene delivery vehicles would look like or how they would function. There are no relevant working examples directed to non-adenoviral vectors comprising a dendrite-specific ligand. Within the adenoviral fibers tested in the instant specification, the only fibers shown to provide a tissue tropism for dendritic cells were obtained from Ad11, Ad16, Ad35, Ad51 or Ad40L. The structural characteristics of the fiber that provide for the dendrite-specific tropism are not described so that one of skill could readily envision the structural characteristics of the fiber that allow these fibers to bind dendritic cells where other adenoviral fibers do not (e.g. Ad5). Therefore, there is no structural, functional basis provided by the instant specification to envision other types of adenoviral fiber that will work in the instant invention (i.e. other than Ad11, Ad16, Ad35, Ad51 or Ad40L).

The prior art appears to be silent with regard to chimeric viral capsids comprising protein fragments that are intended to direct the recombinant capsid to dendritic cells. Therefore, the prior art does not offset the deficiencies of the instant specification with regard to envisioning alternatives to the adenoviral capsids described in the instant specification. With regard to describing other adenoviral fibers obtained from sources other than Ad11, Ad16, Ad35, Ad51 or Ad40L, the prior art teaches the relationship between the sequence of a protein and its tertiary structure (in essence the structure which defines its activity), is not well understood and is not

predictable as evidenced by Berendsen (Science. 1998, Vol. 282, pages 642-643; see the entire document). This reference teaches that "Thus, one of the "grand challenges" of high-performance computer-predicting the structure of proteins-acquires much of the flavor of the Holy Grail quest of the legendary knights of King Arthur: It is extremely desirable to possess but extremely elusive to obtain." (Page 643, columns 1-2). The whole reference teaches about the unpredictability in the art concerning protein structure, and failures to make it predictable. Thus, as taught by Berendsen, it is unlikely that the skilled artisan could envision additional adenoviral fibers providing the recited tissue tropism based upon the teachings of the instant specification.

Based upon the great breadth of hybrid viral capsids comprising protein fragments that must provide a specific tissue tropism encompassed by the rejected claims, and given the lack of a structural/functional basis from the instant specification and prior art to envision specific embodiments of the claimed gene delivery vehicle other than an adenoviral capsid comprising heterologous fibers from Ad11, Ad16, Ad35, Ad51 or Ad40L, one of skill would not have been able to envision a sufficient number of alternative embodiments to describe the broadly claimed genus of such vehicles. Therefore, one of skill in the art would have reasonably concluded applicants were not in possession of the broadly claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in that the metes and bounds of the phrase "having been provided with" are not clear. It is unclear whether this is open or closed language, or even that the phrase specifies that the gene delivery vehicle necessarily comprises a tissue tropism for dendritic cells. It appears, upon reading the specification and remaining claims, that the deleting the phrase and inserting the term "comprising" would be appropriate and remedial.

Claims 2, 5-6, 10-12, 20 are vague and indefinite in that the metes and bounds of the words "derived from" are unclear. It is unclear the nature and number of steps required to obtain a "derivative" of a protein from a viral capsid. It would be remedial to delete the term "derived" and substitute the words "obtained", which implies a more direct process of obtaining the protein fragments.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Crystal et al (U.S. Patent No. 6,127,525; see the entire patent).

Crystal et al teach the construction and use of recombinant adenoviral vectors comprising heterologous fiber proteins wherein all or a portion of the fiber native to the adenoviral capsid has been replaced with the fiber of an adenovirus of a different serotype (e.g. column 11, lines 3-7, or lines 48-62). The chimeric adenoviral capsid has a decreased ability or inability to be recognized by a neutralizing antibody directed against the corresponding wildtype capsid (e.g. Abstract). The adenoviral vector can be of serotype group C (e.g. Ad2 or Ad5), serotype serotype group B, or serotype group F (e.g. Ad40 or Ad41). The vector can be replication competent, or can comprise altered genetic material such that the virus is replication deficient (e.g. column 15, lines 9-34). Any one of the serotypes of human or nonhuman adenovirus can be used as the source of the coat protein, or its gene or coding sequence. Optimal sources include Ad11, Ad16 and Ad35 (e.g. column 4, lines 33-41). Examples are described wherein a minimal adenoviral reporter vector is used to assess the efficiency of cell transduction by the chimeric adenoviral particles of the invention (e.g. Example 2).

The instant specification discloses embodiments wherein the native fiber protein has been replaced with a fiber protein obtained from Ad11, Ad16 or Ad35 and that the chimeric capsids comprising these fibers. Embodiments of inventions taught by Crystal et al featuring capsids comprising entire fibers obtained from Ad11, Ad16 or Ad35 would necessarily be expected to comprise at least a tropism for dendritic cells.

Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a

novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr.
Examiner
Art Unit 1636

Ggl
December 12, 2002